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USPT	antisense or anti-sense or anti sense	8819	<u>L5</u>
USPT	11 or 12	3174	<u>L4</u>
USPT	nitricoxide synthase	()	<u>L3</u>
USPT	inos	2792	<u>L2</u>
USPT	nitric oxide synthase	474	Ll

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L7 Entry 2 of 5

Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830848 A

TITLE: Method and agents for inducement of endogenous nitric oxide synthase for control and management of labor during pregnancy

File: USPT

DRPR:

FIG. 14 is a photograph of in situ hybridization with a rat iNOS cDNA antisense probe for localization of iNOS expression in the pregnant rat uterus at day 16 (FIG. 14A); in the decidua basalis (FIG. 14B), in myocytes (FIGS. 14C and 14D).

DEPR:

The augmentation of uterine NO production is achieved by administration of agents ennancing the capacity of the uterus to make endogenous uterine NO. Such endogenous uterine NO production constituting endogenous tocolytic effect is achieved through auministration of agents having a uterine-selective effect on iNOS in the myometrium. Such agents include systemically or by any other conventional route administered sytokines, growth factors, or sense or antisense oligonuslectides. Exemplary sytokines are Inf. gamma., IL-1.beta., IL-6, IL-8, TNF-.alpha., CSF-1, GM-CSF and TGF-.beta.. Exemplary growth factors are epidermal growth factor (EGF), fibroblast growth factors (FGFs), eicosanoids, alone or in combination with hormones such as progesterone or estradiol 17.beta., of which the levels are very high in pregnancy acting as an adjuvant. Exemplary sense or antisense oligonucleotides are antisense oligonucleotides irested against iNOS gene promoter repressor elements, or sense cligonucleotides directed towards iNOS gene promoter or promoters of genes for iNOS gene transcriptional regulators, which selectively increase uterine NO production. These agents are also delivered to the uterus in a targeted manner, for example, by complexing these agents with other biomolecules, such as hormones, antibodies, or nutrients, which are selectively taken up by or concentrated within the uterus or myometrium. Specific examples of these targeting techniques are complexing an agent with an oxytocin receptor antagenist, complexing an agent with an antibody directed to a uterine-specific antigen, and using liposomal carriers to deliver agents.

DEPR:

The all above discussed results of in vitro studies support the current invention and confirm results of in vivo studies which show that nitric oxide is directly involved in maintaining uterus relaxation during pregnancy. When the endogenous levels or availability of nitric oxide decrease, the uterus respond with increased contractility resulting in labor. When this occurs prior to normal term of pregnancy, such decreased level of nitric oxide results in preterm labor. By providing exagenous nitric oxide source or donor, the preterm contractions can be inhibited and the preterm labor stopped before resulting in preterm delivery. By providing agents hormones such as cytckines growth factors or sense or antisense oligonucleotides, the level of iNOS expression can be enhanced to prevent development or reverse onset of or stop premature labor.

MEFR:

For endogenous control of preterm labor through induction of increased production of N by increased expression of iNOS, hormones, cytokines, growth factors, or sense of antisense oligonucleotides are administered in any suitable route described above.

McGarry, Sean

To:

STIC-ILL

Subject:

reference request

Importance:

High

Please forward the following references to Sean McGarry AU 1635 CM1 11D07

L12 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2000 ACS

AN 1996:324381 CAPLUS

DN 125:54131

TI A first stable inducible ***nitric*** ***oxide*** ***synthase***

antisense macrophage cell line

AU Bosse, Geraldine; Fischer, Hans-Georg; Rothe, Helga

CS Diabetes Research Institute, Heinrich-Heine University, Duesseldorf, 40225, Germany

SO Portland Press Proc. (1996), 10(Biology of Nitric Oxide Part 5), 142 CODEN: POPPEF

DT Journal

LA English

L12 ANSWER 67 OF 79 BIOSIS COPYRIGHT 2000 BIOSIS

AN 1996:255108 BIOSIS

DN PREV199698811237

TI Inducible ***nitric*** ***oxide*** ***synthase***: The use of ***antisense*** oligodeoxynucleotides to study its regulation and role in neoplastic transformation.

AU Lesoon-Wood, L. A.; Lau, A. F.; Cooney, R. V.

CS Mol. Carcinogenesis, Cancer Res. Cent., Honolulu, HI 96813 USA

SO Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 145.

Meeting Info : 87th Annual Meeting of the American Association for Cancer Canada (1996) Proceedings of the American Association for Cana

Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996 ISSN: 0197-016X.

DT Conference

LA English

L12 ANSWER 61 OF 79 MEDLINE

DUPLICATE 28

AN 97144252 MEDLINE

1.1

DN 97144252

TI Evidence for a physiological role for nitric oxide in the regulation of the LH surge: effect of central administration of ***antisense*** oligonucleotides to ***nitric*** ***oxide*** ***synthase***.

AU Aguan K; Mahesh V B; Ping L; Bhat G; Brann D W

CS Department of Physiology and Endocrinology, Medical College of Georgia,

anarode Myz RON objection

Df Journal; Article: (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199706 EW 19970601

L12 ANSWER 60 OF 79 MEDLINE

DUPLICATE 27

AN 96295522 MEDLINE

DN 96295522

TI ***Antisense*** evidence for two functionally active forms of ***nitric*** ***oxide*** ***synthase*** in brain microvascular endothelium.

AU Rosenblum W I; Murata S

CS Department of Pathology (Neuropathology), Medical College of Virginia/Virginia Commonwealth University, Richmond 23298-0017, USA.

NC HL35935 (NHLBI)

SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Jul 16) 224 (2) 535-43.

Journal code: 9Y8. ISSN: 0006-291X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199611

L12 ANSWER 43 OF 79 MEDLINE

DUPLICATE 19

AN 97368347 MEDLINE

DN 97368347

TI Functionally differentiating two neuronal ***nitric*** ***oxide***

synthase isoforms through ***antisense*** mapping: evidence for opposing NO actions on morphine analgesia and tolerance.

AU Kolesnikov Y A; Pan Y X; Babey A M; Jain S; Wilson R; Pasternak G W

CS The Cotzias Laboratory of Neuro-Oncology and Departments of Neurology and Anesthesiology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.

NC DA07242 (NIDA)

DA00220 (NIDA)

DA00296 (NIDA)

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Jul 22) 94 (15) 8220-5.

Journal code: PV3. ISSN: 0027-8424.

L12 ANSWER 42 OF 79 CAPLUS COPYRIGHT 2000 ACS

AN 1997:168560 CAPLUS

DN 126:152830

TI Vascular endothelial growth factor receptor gene regulator screening, antisense and gene therapy, and cancer inhibitors, antiarteriosclerotics, and angiogenesis regulation

IN Patterson-Winston, Campbell; Lee, Mu-En; Haber, Edgar

PA President and Fellows of Harvard College, USA

SO PCT Int. Appl., 69 pp.

CODEN PIXXD2

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WO 1996-US10725 19960621 PI WO 9700957 A1 19970109 W: AU, CA, IL, JP, MX, NO RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5888765 A 19990330 US 1995-494282 19950623 CA 1996-2225460 19960621 AA 19970109 CA 2225460 AU 9662884 A1 19970122 AU 1996-62884 19960621 A1 19980408 EP 1996-921746 19960621 EP 833907

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 11509088 T2 19990817 JP 1996-503975 19960621

PRAI US 1995-494282 19950623 US 1995-573692 19951218 WO 1996-US10725 19960621